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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,032	02/05/2004	Frank D. Lee	EPT-001C2	5991

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EXAMINER	
LIN, JERRY	

ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
12/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/773,032	LEE ET AL.	
	Examiner	Art Unit	
	JERRY LIN	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-8,13,19-21,23,24,26-28,30-34,42 and 44-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-8, 13, 19-21, 23, 24, 26-28, 30-34, 42, 44-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 16, 2008 has been entered.

Status of the Claims

Claims 1-4, 6-8, 13, 19-21, 23, 24, 26-28, 30-34, 42, and 44-47 are under examination.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1, 3-4, 19, 24, 26, 28, 30-34, 42, 44, 46, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dours-Zimmermann et al. (The Journal of Biological Chemistry (1994) Volume 269, Number 52, pages 32992-32998) in view of Hongo et al. (Journal of General Virology (1994) Volume 75, pages 3503-3510) in view of Jemmerson (Proc. Natl. Acad. Sci. (1987) Volume 84, pages 9180-9184) in view of Arenkov et al. (Analytical Biochemistry (2000) Volume 278, pages 123-131).

The instant methods are drawn to a method of detecting and quantifying target proteins in a sample by fragmenting proteins in a sample, exposing the fragmented proteins to an addressable array of capture agents, wherein the capture agent binds to a PET that comprises the amino acid sequence encoded by the RNA spanning a splice junction and using a secondary capture agent labeled with a detectable moiety to detect a captured fragment.

Regarding claims 1, 30, 42, and 48, Dours-Zimmermann et al. teach a method of fragmenting proteins using a predetermined proteolytic protocol (page 32993, left column bottom) wherein the protein fragments contain epitopes that are unambiguously indicative of the presence of a sample of the target proteins and comprise the amino

acid sequence encoded by the RNA with a splice junction (page 32995); creating antibodies (capture agents) that selectively interact with the epitopes (page 32995) and contacting the antibodies with the protein fragments (page 32995) to detect the presence or absence of the target proteins (page 32995).

However, Dours-Zimmermann et al. do not teach wherein the amino acid sequence encoded by the RNA spans the splice junction.

Hongo et al. disclose synthesizing unspliced and spliced mRNAs from the same segment of RNA that contains a splice junction and translating those mRNAs to yield proteins (abstract; page 3503, left column). Furthermore, Hongo et al. teach detecting polypeptides encoded by mRNA using a molecular assay (abstract).

However, neither Dours-Zimmermann et al. do nor Hongo et al. teach wherein the proteins are denatured.

Regarding claims 1, 30, 42, and 48, Jemmerson teaches creating peptide fragments by a denaturation and proteolytic process (page 9180, right column-page 9181, left column); creating antibodies specific for the peptide fragments, and using the created antibodies to detect the peptide fragments in an assay (page 9181, left column; page 9182, right column).

However, Dours-Zimmermann, Hongo et al. and Jemmerson do not teach presenting the antibodies (i.e., capture agents) in an array format.

Regarding claims 1, 30, 42, and 48, Arenkov et al. teach presenting antibodies in an array format and using a secondary capture agent to detect the target protein (abstract; page 126, right column – page 127, left column, top); wherein the secondary

capture agent labeled with a fluorophore binds to an epitope separate from the solvent accessible binding surfaces (abstract; page 126, right column – page 127, left column, top).

Regarding claims 3-4, 24, 33, 34, and 46, Arenkov et al. teach wherein the capture agent is a antibody or a non-antibody (page 126); wherein the secondary capture agent labeled with a fluorophore binds to an epitope separate from the solvent accessible binding surfaces (abstract; page 126, right column – page 127, left column, top).

Regarding claim 26, Dours-Zimmermann teaches extracting the target proteins from whole cell lystate, which would include a billion molar excess of unrelated proteins or fragments relative to the target protein (page 32993, left column bottom).

Regarding claims 19 and 28, Dours-Zimmermann teaches wherein the cells are grown in an artificial environment (page 32993, left column, under "Cell Cultures"); and where the target protein may be a biomarker for a splice variant (abstract).

Regarding claims 31-32, Arenkov et al. teach wherein the solid support in disposed in a manner that encodes the identity of the capture agents (i.e., an addressable array) (abstract); wherein there are 2-100 or more different capture agents (abstract; page 125, left column bottom).

Regarding claim 44, Arenkov et al. teach wherein the array of capture agents interacts with different epitopes (page 126).

All the elements of the instant claimed method and instant claimed array are known in the references by Dours-Zimmermann et al., Hongo et al., Jemmerson, and

Arenkov et al. Each of the references teach methods of detecting a polypeptide or protein of interest. The only difference between the claimed invention and the recited reference is that the claimed invention is the combination of these old elements into a single method or array. Furthermore, one of ordinary skill in the art would have the reasonable expectation that the combination of these teachings would allow the detection of a protein or peptide fragment translated from an RNA spanning a splice junction. Thus, it would have been obvious to one of ordinary skill in the art to combine the methods of Dours-Zimmermann et al., Hongo et al., Jemmerson, and Arenkov et al., because the method taught by each reference is not dependent on the other methods, and the combination of the methods may be performed to achieve predictable results of detecting the presence or absence of proteins encoded by RNA spanning a splice junction.

Response to Arguments

4. Applicants have responded to this rejection by stating that Hongo et al. does not teach antibodies specific to an amino acid sequence that is encoded by an RNA splice junction. However, the instant claims recites that the PET comprises an amino acid sequence encoded by an RNA spanning an splice junction. While one interpretation of the claim language includes embodiments where the PET includes those amino acids that correspond to the RNA at the splice junction itself, another interpretation of the of the claim language is drawn to where the PET may be anywhere on the protein which is encoded by an RNA that spans the splice junction. In other words, as the claims are written, the PET is not required to include those amino acids that directly correlate to the

RNA at the splice junction itself. Hongo et al. teach using antibodies that detect proteins that are encoded by RNA which span a splice junction. Thus, Hongo et al. teach this limitation. This rejection is maintained.

5. Claims 2, 6-8, 13, 20, 21, 23, 26, 27, 45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dours-Zimmermann et al. (The Journal of Biological Chemistry (1994) Volume 269, Number 52, pages 32992-32998) in view of Hongo et al. (Journal of General Virology (1994) Volume 75, pages 3503-3510) in view of Jemmerson (Proc. Natl. Acad. Sci. (1987) Volume 84, pages 9180-9184) in view of Arenkov et al. (Analytical Biochemistry (2000) Volume 278, pages 123-131) as applied to claims 1, 3-4, 19, 24, 28, 30-34, 42, 44, 46 and 48 above, and further in view of Wagner et al. (US 6,897,073 B2).

The instant methods are drawn to a method of detecting and quantifying target proteins in a sample by fragmenting proteins in a sample, exposing the fragmented proteins to an addressable array of capture agents, wherein the capture agent binds to a PET that comprises the amino acid sequence encoded by the RNA spanning a splice junction and using a secondary capture agent labeled with a detectable moiety to detect a captured fragment.

Dours-Zimmermann et al., Hongo et al, Jemmerson, and Arenkov et al. are applied as above.

However, neither Dours-Zimmermann et al., Hongo et al., Jemmerson, nor Arenkov et al. teaches determining the amount of target protein in the sample by averaging the results obtained from each said capture agent.

Regarding claims 2, 20, 21, and 45, Wagner et al. also teach a method of detecting proteins using arrays of protein-capture agents (abstract) which includes contacting the array with cleaved or denatured protein analytes (membrane bound proteins) from body fluids (column 35, lines 22-44) and quantifying the amount of a target protein by averaging the result (including if the total amount of the detected proteins is averaged by one spot in the array) (column 35, line 63-column 36, line 23; column 39, lines 12-50).

Regarding claims 6 and 47, Wagner et al. teach arrays with capture agents bind to the same PET (column 12, line 14 - column 13, line 30); furthermore, Wagner et al. teach finding proteins that bind to the same PET at different affinities (column 30, line 54 – column 34, line 45).

Regarding claims 7 and 8, Wagner et al. teach using cellular extracts which would contain multiple forms of protein such as pro-form or mature form proteins (column 35, lines 22-44).

Regarding claims 13, Wagner et al. teach detecting protein fragments (processed forms) of cellular extracts and determining the ratio of one form of protein to another form (column 45, lines 32-39; column 38, lines 43-65).

Regarding claim 23, Wagner et al. teach wherein a secondary capture agent may be used for detection using fluorescent methods (column 36, lines 24-57).

Regarding claim 27, Wagner et al. teach wherein the PET is identified based on a sequenced genome (column 30, lines 42-54).

All the elements of the instant claimed method and instant claimed array are known in the references by Dours-Zimmermann et al., Hongo et al., Jemmerson, Arenkov et al., Wagner et al. Each of the references teaches methods of detecting a polypeptide or protein of interest. The only difference between the claimed invention and the recited reference is that the claimed invention is the combination of these old elements into a single method or array. Furthermore, one of ordinary skill in the art would have the reasonable expectation that the combination of these teachings would allow the detection of a protein or peptide fragment translated from an RNA spanning a splice junction. Thus, it would have been obvious to one of ordinary skill in the art to combine the methods of Dours-Zimmermann et al., Hongo et al., Jemmerson, Arenkov et al., and Wagner et al., because the method taught by each reference is not dependent on the other methods, and the combination of the methods may be performed to achieve predictable results of detecting the presence or absence of encoded by RNA spanning a splice junction.

Response to Arguments

6. Applicants have responded to this rejection by presenting arguments against Hongo et al. See above for the Examiner's response.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JERRY LIN whose telephone number is (571)272-2561. The examiner can normally be reached on 7:00-5:30pm, M-TH.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie A. Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jerry Lin/
Examiner, Art Unit 1631
12/7/08